

In the Claims

Please amend the claims as follows:

Claim 1 (Previously Amended): A high-throughput method of screening compounds capable of modulating topoisomerase activity comprising:

- (a) incubating at least a first nucleic acid, a topoisomerase and a potential topoisomerase-modulating compound, wherein the nucleic acid comprises at least one tag, and
- (b) assaying for a nucleic acid religation product.

Claim 2 (Original): The method of claim 1, wherein the nucleic acid is DNA.

Claim 3 (Original): The method of claim 1, wherein the nucleic acid is RNA.

Claim 4 (Original): The method of claim 1, wherein the at least one tag is a detection tag or an affinity tag.

Claim 5 (Original): The method of claim 1, wherein the method comprises incubating at least a first nucleic acid and a second nucleic acid.

Claim 6 (Original): The method of claim 5, wherein the second nucleic acid is a religation strand comprising oligonucleotides operatively associated with at least one marker tag.

Claim 7 (Original): The method of claim 6, wherein the first nucleic acid is operatively associated with an affinity tag and the second nucleic acid is operatively associated with a detection tag.

Claim 8 (Currently Amended): The method of claim 1, wherein the assay detects ~~for~~ topoisomerase inhibitors.

Claim 9 (Currently Amended): The method of claim 1, wherein the assay detects ~~for~~ topoisomerase activators.

Claim 10 (Original): The method of claim 1, wherein the topoisomerase is a Type I or Type III topoisomerase.

Claim 11 (Original): The method of claim 1, wherein the topoisomerase is a Type II or Type IV topoisomerase.

Claim 12 (Original): The method of claim 1, wherein assaying comprises measuring the level of nucleic acid religation activity in the presence and absence of the topoisomerase-modulating compound.

Claim 13 (Currently Amended) The method of claim 1, wherein the level of religation activity is inversely proportional to the effectiveness of the topoisomerase ~~inhibitory~~ modulating compound.

Claim 14 (Original): The method of claim 1, wherein step (a) is performed on a solid support.

Claim 15 (Original): The method of claim 1, wherein step (a) is performed in a liquid phase.

Claim 16 (Original): The method of claim 1, wherein the nucleic acid and topoisomerase are covalently complexed, wherein the topoisomerase retains its religation activity.

Claim 17 (Withdrawn): A method of treating cancer comprising administering a pharmaceutical composition comprising a topoisomerase inhibitor to a patient in need thereof.

Claim 18 (Withdrawn): A method of treating an infection by a pathogen comprising administering a pharmaceutical composition comprising a topoisomerase inhibitor to a patient in need thereof.

Claim 19 (Withdrawn): The method of claim 18, wherein the pathogen is a virus, bacterium, fungus or parasite.

Claim 20 (Withdrawn): A kit for screening compounds that modulate topoisomerase religation activity comprising:

- (a) a substrate nucleic acid comprising a first tag,
- (b) a religation nucleic acid comprising a second tag and a 5'-OH,
- (c) a topoisomerase, and
- (d) a means for measuring a covalently linked product comprising (a) and (b) in a test mixture comprising (a), (b) and (c) in the presence or absence of a topoisomerase-modulating compound.

Claim 21 (Withdrawn): S. Taniguchi, H. Fujiki, H. Kobayashi, H. Go, K. Miyado, H. Sadano and R. Shimokawa. 1992. Effect of (-)-epigallocatechin gallate, the main constituent of green tea, on lung metastasis with mouse B16 melanoma cell lines. *Cancer Letters* **65**, 51-54.

Claim 22 (Previously Added): A method to identify a compound that modulates topoisomerase activity comprising:

- (a) incubating a reaction mixture comprising a substrate nucleic acid, a religation strand, a topoisomerase, and a candidate compound; and
- (b) assaying for ligation of the substrate nucleic acid and the religation strand.

Claim 23 (Previously Added): A method to identify a compound that modulates topoisomerase activity comprising:

- (a) incubating a reaction mixture comprising a substrate nucleic acid, a topoisomerase, and a candidate compound; and
- (b) assaying for intramolecular ligation of the substrate nucleic acid to form a hairpin, a circular nucleic acid, or a multimer of the substrate nucleic acid.